

What Is Claimed Is:

- Claim 1. A compound, comprising an N36 peptide variant or a derivative or pharmaceutically acceptable salt thereof, wherein said compound inhibits the fusion of HIV-1 to a human cell.
- 5 Claim 2. The compound of claim 1, wherein:
- (A) the identities of the amino acid residues occupying the "e" and "g" positions of said N36 peptide variant are at most 89% identical to the amino acid residues occupying the "e" and "g" positions of N36 (SEQ ID NO:1), and
- 10 (B) the identities of the amino acid residues occupying the "non-e" and "non-g" positions of the N36 peptide variant are at least 70% identical to the amino acid residues occupying their counterpart positions in the N36 peptide;
- wherein said N36 peptide variant possesses the ability to disrupt the internal trimeric coiled-coil of N-helices of gp41.
- 15 Claim 3. The compound of claim 1, wherein said N36 peptide variant differs in amino acid sequence from the sequence of N36 peptide (SEQ ID NO:1), by at least a substitution of an amino acid residue selected from the group consisting of: V₄, Q₆, L₁₁, A₁₃, Q₁₈, L₂₀, V₂₅, G₂₇ and
- 20 Q₃₂, wherein the letters V, Q, L, A and G denote Valine, Glutamine, Leucine, Alanine and Glycine, respectively, and the number denotes the position of the residue in SEQ ID NO:1.
- Claim 4. The compound of claim 3, wherein said N36 peptide variant differs in amino acid sequence from SEQ ID NO:1, by at least a
- 25 substitution of at least two of said amino acid residues V₄, Q₆, L₁₁, A₁₃, Q₁₈, L₂₀, V₂₅, G₂₇ and Q₃₂.
- Claim 5. The compound of claim 4, wherein said N36 peptide variant differs in amino acid sequence from SEQ ID NO:1, by at least a

substitution of at least four of said amino acid residues V₄, Q₆, L₁₁, A₁₃, Q₁₈, L₂₀, V₂₅, G₂₇ and Q₃₂.

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Claim 6. The compound of claim 5, wherein said N36 peptide variant differs in amino acid sequence from SEQ ID NO:1, by at least a substitution of at least five of said amino acid residues V₄, Q₆, L₁₁, A₁₃, Q₁₈, L₂₀, V₂₅, G₂₇ and Q₃₂.

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Claim 7. The compound of claim 6, wherein said N36 peptide variant differs in amino acid sequence from SEQ ID NO:1, by at least a substitution of said amino acid residues V₄, Q₆, L₁₁, A₁₃, Q₁₈, L₂₀, V₂₅, G₂₇ and Q₃₂.

Claim 8. The compound of claim 7, wherein said N36 peptide variant has the amino acid sequence of N36^{Mut(e,g)} (SEQ ID NO:3):
SGIDQEQNNL TRLEAQIHE LQLTQWKIKQ LLARIL.

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Claim 9. A pharmaceutical composition comprising a therapeutically effective amount of an N36 peptide variant or a derivative or pharmaceutically acceptable salt thereof, wherein said compound inhibits the fusion of HIV-1 to a human cell, in admixture with a pharmaceutically acceptable excipient.

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Claim 10. The pharmaceutical composition of claim 9, wherein:
(A) the identities of the amino acid residues occupying the "e" and "g" positions of said N36 peptide variant are at most 89% identical to the amino acid residues occupying the "e" and "g" positions of N36 (SEQ ID NO:1), and
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(B) the identities of the amino acid residues occupying the "non-e" and "non-g" positions of the N36 peptide variant are at least 70% identical to the amino acid residues occupying their counterpart positions in the N36 peptide;

wherein said N36 peptide variant possesses the ability to disrupt the internal trimeric coiled-coil of N-helices of gp41.

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Claim 11. The pharmaceutical composition of claim 9, wherein said N36 peptide variant differs in amino acid sequence from the sequence of N36 peptide (SEQ ID NO:1), by at least a substitution of an amino acid residue selected from the group consisting of: V₄, Q₆, L₁₁, A₁₃, Q₁₈, L₂₀, V₂₅, G₂₇ and Q₃₂, wherein the letters V, Q, L, A and G denote Valine, Glutamine, Leucine, Alanine and Glycine, respectively, and the number denotes the position of the residue in SEQ ID NO:1.

Claim 12. The pharmaceutical composition of claim 11, wherein said N36 peptide variant differs in amino acid sequence from SEQ ID NO:1, by at least a substitution of at least two of said amino acid residues V₄, Q₆, L₁₁, A₁₃, Q₁₈, L₂₀, V₂₅, G₂₇ and Q₃₂.

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Claim 13. The pharmaceutical composition of claim 12, wherein said N36 peptide variant differs in amino acid sequence from SEQ ID NO:1, by at least a substitution of at least four of said amino acid residues V₄, Q₆, L₁₁, A₁₃, Q₁₈, L₂₀, V₂₅, G₂₇ and Q₃₂.

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Claim 14. The pharmaceutical composition of claim 13, wherein said N36 peptide variant differs in amino acid sequence from SEQ ID NO:1, by at least a substitution of at least five of said amino acid residues V₄, Q₆, L₁₁, A₁₃, Q₁₈, L₂₀, V₂₅, G₂₇ and Q₃₂.

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Claim 15. The pharmaceutical composition of claim 14, wherein said N36 peptide variant differs in amino acid sequence from SEQ ID NO:1, by at least a substitution of said amino acid residues V₄, Q₆, L₁₁, A₁₃, Q₁₈, L₂₀, V₂₅, G₂₇ and Q₃₂.

- Claim 16. The pharmaceutical composition of claim 15, wherein said N36 peptide variant has the amino acid sequence of N36^{Mut(e,g)} (SEQ ID NO:3): SGIDQEQNNL TRLIEAQIHE LQLTQWKIKQ LLARIL.
- 5 Claim 17. The pharmaceutical composition of claim 9, wherein said composition additionally contains an HIV protease inhibitor, an HIV reverse transcriptase inhibitor, an HIV integrase inhibitor, or an HIV fusion inhibitor.
- 10 Claim 18. A method of treating HIV infection that comprises providing to a recipient a therapeutically effective or a prophylactically effective amount of a pharmaceutical composition comprising a therapeutically effective amount of an N36 peptide variant or a derivative or pharmaceutically acceptable salt thereof, wherein said compound inhibits the fusion of HIV-1 to a human cell, in admixture with a pharmaceutically acceptable excipient.
- 15 Claim 19. The method of claim 18, wherein said N36 peptide variant has the amino acid sequence of N36^{Mut(e,g)} (SEQ ID NO:3): SGIDQEQNNL TRLIEAQIHE LQLTQWKIKQ LLARIL.
- 20 Claim 20. The method of claim 18, wherein said pharmaceutical composition additionally contains an HIV protease inhibitor, an HIV reverse transcriptase inhibitor, an HIV integrase inhibitor, or an HIV fusion inhibitor.